REMARKS AND ARGUMENTS

Reconsideration of the application is respectfully requested.

Claims 1, 2, and 5-62 are presently pending in this application. Claims 1, 2, 7, and 48 are amended. Claims 61- 62 are new.

No new matter has been added to the claims. The amendments to claims 1, 2, and 48 change only the syntax of the claims. The amendment in claim 7 is to correct a typographical error in the moiety R^C. New claim 61 is directed to subject matter found in the provisional application (page 8, line 1 to page 10, line 9 for the macrolide and page 11, line 8 to the end of the page for the steroid) and is supported in the present application in claim 1 as originally filed. Support for the terms R^P and OR^P can be found in the provisional application on page 10 lines 8 - 20 as well as in the structural formulas for the macrolide sugar groups that encompass explicitly both hydroxyl and amine protective groups (pages 8 - 9). New claim 62 is directed to subject matter exemplified in the provisional application. Support for this claim can be found in the provisional application compounds 1 – 33 (pages 51 – 76) as well as at p.8, line 1 - p.10, line 9 and p.11, lines 8 *et seq.* of the provisional application.

35 U.S.C. §102(a)

The Examiner has rejected claims 1, 2, 5 - 7 and 48 - 60 under 35 U.S.C§102 (a) as being anticipated by Burnet et al. (US 2004/0087517). The Burnet '517 application was filed on February 14, 2003 and claims priority to provisional application US 60/357,434, filed Feb. 15, 2002. It was published on May 6, 2004.

This rejection is respectfully traversed. The Burnet '517 application is not available under 35 U.S.C§102(a) since subject matter disclosed by Burnet was not known or used by others in this country, or described in a printed publication in this or a foreign country, before the invention described by claims 1, 2, and 5 – 62. Burnet '517 was published on May 6, 2004, after the filing date of the present non-provisional application (July 8, 2003), therefore later than the present priority date (July 8, 2002), and there is no indication that the subject matter of Burnet '517 was known or used in this country before the present invention.

35 U.S.C. §102(e)

1. The present invention antedates Burnet '517

The Examiner has rejected claims 1, 2, and 5 – 60 under 35 U.S.C§102 (e) as being anticipated by Burnet et al. (US 2004/0087517). The priority date of the present application is July 8, 2002 based on provisional application 60/394,670. It thus antedates any disclosure in the Burnet non-provisional '517 application filed February 14, 2003.

The priority document of the present application contains 33 actual examples and discloses the preparation of 33 conjugates that were reduced to practice no later than July 8, 2002 and support the present claims.

Moreover, a number of the conjugates, at least compounds 1, 4, 9, 19, 23, and 27, were made and characterized on or before February 15, 2002, the priority date that the Burnet application asserts. They thus antedate any disclosure of the Burnet provisional application. The pre-February 15, 2002 synthesis and characterization of these compounds and the diligent synthesis and characterization of several other compounds are supported by the accompanying §1.131 declaration by Linda Tomašković, one of the inventors.

The early synthesis and characterization of at least Compounds 1, 4, 9, 19, 23 and 27, demonstrates that the present invention was conceived prior to February 15, 2002, and actually reduced to practice prior to February 15, 2002 and this activity continued and expanded thereafter until the provisional application was filed on July 8, 2002. As filed, the provisional application contains 33 working examples (Examples 1-33), including the compounds described in declaration Exhibits B – I. This demonstrates that the inventors diligently worked to synthesize and test additional conjugates from prior to February 15, 2002 until the filing of provisional application 60/394,671 and thereafter until the filing date of the present application.

From a date prior to February 15, 2002, compounds of the present invention were understood to have anti-inflammatory activity. As stated in the Tomašković declaration and its Exhibit A, the assignee of the present application had an on-going program in place addressing anti-inflammatory conjugates since before February 15, 2002. Conjugates of macrolides and compounds having anti-inflammatory activity having an "anti-inflammatory subunit that can be steroid or nonsteroid" (Declaration Exhibit A pg 4: 2-3) were being developed by the assignee no later than

January 3, 2002 for their anti-inflammatory activity. Therefore, the anti-inflammatory utility of compounds such as those of the present invention was known or at the very least contemplated prior to February 15, 2002.

Thus, the attached declaration by Linda Tomašković details the conception and reduction to practice of the present invention prior to the filing of the Burnet provisional application. Exhibits B-I to this declaration are the pages of the laboratory notebooks (and their English translation) recording the synthesis and characterization (by mass spectrometry and HPLC) of compounds made prior to February 15, 2002. This evidence demonstrates that the present inventors had conceived and reduced the invention to practice before the Burnet provisional application was filed. Further, the scope of the provisional patent application from which the present application as filed shows further that the Inventors diligently worked on this invention, as declarant testifies, from conception to the filing of the provisional application.

We note that it is not necessary for the applicants to show reduction to practice of the entire scope of the invention. The §131 declaration "must establish possession of either the whole invention claimed or something falling within the claim (such as a species of a claimed genus), in the sense that the claim as a whole reads on it." MPEP 715.02 citing *In re Tanczyn* , 347 F.2d 830, 146 USPQ 298 (CCPA 1965).

Therefore, since the present invention was both conceived and reduced to practice prior to the filing date of either of the Burnet provisional or non provisional patent application, the rejection under 35 U.S.C§102(e) based on the Burnet application has been overcome and its withdrawal is respectfully requested.

2. The Burnet provisional application fails to disclose the claimed compounds

Moreover, there is another independent reason why an anticipation rejection based on Burnet is improper and should be withdrawn. The Burnet provisional application fails to disclose any conjugates within claims 1, 2, 5-7 or 31-45. Furthermore, the general disclosure of conjugates of "transportophores" and "nonantibiotic therapeutic agents" of Burnet contains no teaching of the claimed compounds. According to the Burnet provisional application, a "transportophore" can

encompass a variety of molecules, including broad classes of compounds such as alcohols and organic acids. Specifically, transportophores are described in the provisional Burnet specification at page 3 line 23 to page 4 line 2 as follows:

> The transportophore can be a metabolite (such as an amino acid or peptide), a natural product, a metabolite derivative (e.g., a sugar, amino, or peptide derivative), an organic acid an organic base, a nucleobase, or an alcohol. It can be an amphiphilic molecule having a pKa value of 6.5 to 9.5, or a cyclic or heterocyclic molecule (e.g., lactone, lactam, ether, cyclic acetal or hemi-acetal). The cyclic or heterocyclic molecule can have an attached sugar. The cyclic or heterocyclic molecule can be a macrolactone or macroether, including a macrolactone or macroether having an attached sugar. The cyclic or heterocyclic molecule can also be a macrolide or ketolide having an amino sugar, including a macrolide having mono-, di-, or tri-basic groups (e.g., an amine).

The term, "therapeutic agent," is introduced in the Burnet provisional at page 31, lines 12-15, as follows:

> A "therapeutic agent," as used herein, is a molecule with pharmacological activity (e.g., a therapeutic agent, medicine, medicament, or active agent), a disease modification agent, or any other molecule that can be covalently attached to a transportophore via a bond or a linker which may have a desirable mode of action in immune cell.

Thus, both "transportophore" and "therapeutic agent" are defined very broadly and cannot be deemed to disclose specifically the conjugates of the specific macrolides of the present claims and the steroids of the present claims. Even though some lists of classes of transportophores and classes of therapeutic agents are provided, there is no specific guidance to pair any transportophores structurally related to the macrolides of the present invention with any steroids structurally related to those of the present invention. Accordingly, the generic disclosure of the Burnet provisional application does not disclose and therefore cannot anticipate the subject matter of the present claims.

Nor do the specific examples of the Burnet provisional application cure the deficiency of its general disclosure. None disclose conjugates containing a steroid moiety, nor any steroids are exemplified, much less those claimed in the present claims. For these additional reasons, there is no anticipation by the Burnet provisional application.

Claim 1

Accordingly, Burnet does not anticipate claim 1 under 35 U.S.C. § 102(e) for the reasons given above.

Claim 2

Since claim 1 is not anticipated, it follows that independent claim 2, which is narrower than but entirely within the scope of claim 1, is not anticipated either.

Claims 5-7

Since claim 2 is not anticipated, it follows that still narrower claims 5-7 dependent on claim 2, are not anticipated either.

Claims 8 - 47

These claims are not rejected under 35 U.S.C §102.

Claim 48

Since Burnet does not anticipate the product claim as discussed above, the subject matter of claim 48, a process for making the novel conjugates describe in claim 1, is also not anticipated. Additionally, Burnet does not disclose the process described in this claim. The Burnet provisional application describes no means for synthesizing macrolide-steroid conjugates, and the four methods described in the regular application are each limited to mixing succinic anhydride with a macrolide and steroid.

Claims 49 and 55

Burnet does not anticipate the pharmaceutical composition claims 49 and 55 since the claimed pharmaceutical compositions are limited to compounds of claim 1 that are not anticipated as shown above, and to derivatives (*e.g.*, salts) of such compounds also not anticipated by Burnet.

Claims 50-54 and 56-60

These claims, drawn to methods of using the compounds of claim 1, are not anticipated by Burnet at least for the reasons that the compounds of claim 1 are not anticipated by Burnet.

Claim 61

Claim 61 is similarly not anticipated by Burnet '517 under 35 U.S.C. § 102(e), not only because it has been removed as a reference under 35 U.S.C. § 102(e) by the present showing of prior invention but also—and independently—because the subject matter of Claim 61 was identically present in the provisional application filed July 8, 2002, (from which the present application claims priority). This filing date is prior to the filing date of Burnet '517. The Burnet provisional application has a filing date of February 15, 2002. However, no compound of the Burnet provisional application is encompassed by Claim 61. As shown above with respect to the other claims any general teaching of the Burnet provisional application is insufficient to anticipate compounds of claim 61.

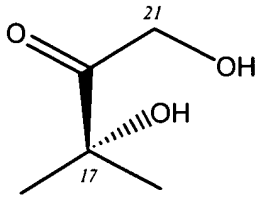
The Burnet provisional application, as discussed above, was filed before the priority date of the present application. However, the Burnet provisional did not disclose even a single macrolide-steroid conjugate and therefore does not disclose and does not specifically teach any compounds encompassed by claim 61.

Claim 62

Since claim 61 is not anticipated, it follows that still narrower claim 62 dependent on claim 61, is not anticipated either.

Anticipation requires that each and every element of the rejected claim be disclosed in a single prior art reference. See, M.P.E.P. § 2131. Every element of the claimed invention must be literally present, arranged as in the claim. *Perkin Elmer Corp. v. Computervision Corp.*, 732 F.2d 888, 894, 221 USPQ 669, 673 (Fed. Cir. 1984). A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Since each element of claim 61 is not provided in a prior art reference, this claim is not anticipated.

Even if the Burnet non provisional ('517) application had been available as a reference under 35 U.S.C. §102(e), it would still not anticipate the present compounds because any steroid conjugates it discloses (compounds 82, 83, 85 and 86) are not encompassed by the present claims for at least the reason that the steroid component is different from the steroids in the present claims. Even though corticosteroids are listed as a general class of therapeutic agents, there is no specific teaching in Burnet '517 that a corticosteroid can be modified to remove the C21 carbon and terminal OH found on the corticosteroid.



Accordingly, the present claims are not anticipated by Burnet, and withdrawal of the rejection is respectfully requested.

35 U.S.C. §103

The Examiner has rejected claims 8 - 47 under 35 U.S.C§103(a) as being unpatentable over Burnet stating that a person of ordinary skill in the art would have been motivated to choose particular corticosteroids and link them to erythromycin derivatives because Burnet teaches that such linkage improves ease of formulation, gastric stability, bioavailability, etc.

Since Burnet is not available as a reference under 35 U.S.C§102(a) or (e), the rejection is respectfully traversed, and reconsideration is requested. Additionally, as will be shown below, the teaching of Burnet is inadequate to disclose or suggest the present compounds. Therefore Applicants respectfully request reconsideration and withdrawal of this rejection.

Independently, Burnet would not have been used to show that a person of ordinary skill in the art would have been motivated to link a steroid and erythromycin derivatives to form the conjugates of the presently claimed invention. Neither the inclusion of corticosteroids within a 2-1/2-column list of therapeutic agents as provided in the provisional application nor the limited four macrolide-corticosteroid conjugates disclosed in Burnet '517 make the use of the claimed steroid conjugates obvious. Additionally, Burnet does not teach steroidal compounds in which the C21

carbon and terminal OH of a corticosteroid is removed and a linker is formed, and for this reason also would not render the present invention obvious.

Moreover, Burnet teaches that "similar molecules with similar properties can exhibit quite different uptake into immune cells" (60/ 357,434, pg 53: 27-28). In Applicant's view, this teaches away from modifying the structures disclosed by Burnet in any manner including one that might yield compounds of the invention, Accordingly, no rejection under §103 is appropriate.

Applicants submit that the presently claimed method is not prima facie obvious over the teaching of Burnet. It is not obvious to conjugate the particular circumscribed class of macrolides as claimed to the claimed steroids based on the teachings of Burnet since Burnet teaches that "similar molecules with similar properties can exhibit quite different uptake into immune cells, hence the difficulty in employing general specifications known in the art" (para. 0728). Burnet does not disclose any macrolide-steroid conjugates other than the four conjugates in the non-provisional application, and does not teach how to obtain the macrolide-steroid conjugates as claimed in the present invention that have uptake into immune cells, therefore, the present claims are not obvious.

Accordingly, in view of the amendments and arguments set forth above, it is respectfully submitted that the claimed subject matter would not have been obvious to one of ordinary skill in the art over Burnet. Applicants respectfully request that the rejections be withdrawn.

The pending claims in this application are believed to be in condition for allowance. The Examiner is therefore respectfully requested to enter this Amendment, and to pass this application to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: January 3, 2006

Respectfully submitted,

By _____

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